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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/762,714	01/22/2004	Maxwell Gordon	1360-001	5204

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EXAMINER	
CLAYTOR, DEIRDRE RENEE	
ART UNIT	PAPER NUMBER
1617	
MAIL DATE	DELIVERY MODE
04/02/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/762,714	GORDON, MAXWELL	
	Examiner	Art Unit	
	Renee Claytor	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 January 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,16-18,21 and 22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6, 16-18, 21-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed on 1/9/2008 is hereby acknowledged.

Applicants have amended claim 6 and cancelled claims 11, 13 and 15. The amendment and cancellation of claims is sufficient to overcome the 35 USC 112, first paragraph rejection over claims 6, 11, 13 and 15 and the rejection is hereby withdrawn.

Applicant's arguments over the 35 USC 102 and 103 rejections over Oshlack et al. have been fully considered. Applicants argue that the specific formulation in newly amended claim 1 is not disclosed in or made obvious by Oshlack et al. Applicants further argue that Oshlack et al. does not teach a three pellet formulation where the pellets are formulated to release the drugs in specific anatomical locations of the small intestines.

In response to the above arguments, it is noted that Oshlack et al. does not exemplify a formulation with every hydrocolloid as listed in claim 1. However, Oshlack et al. teaches the use of the agents in the formulation in the specification. Furthermore, Oshlack et al. teaches compositions with a pellet formulation; therefore, it would be obvious that the composition would be released in the same areas.

Accordingly, the following new grounds of rejections are given below due to Applicants amendments to the claims.

Claim Rejections – 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 22 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of constipation caused by opiates comprising administration of enteric coated opiate antagonist pellets that reduce or eliminate the constipating effects of opioid agonist, does not reasonably provide enablement for the elimination (which the Examiner is interpreting as prevention) of constipation caused by opiates. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

1) The nature of the invention and breadth of the claims: The invention is drawn to a method of reducing or eliminating constipation caused by opiates comprising administration of a solid pharmaceutical dosage form of enteric coated opiate antagonist pellets.

2) The state of the prior art: The start of the art regarding treating opiate induced constipation with naloxone is well known in the art. McNicols et al. (J Pain, Vol. 4, No 5, 2003: p 231-256) review articles in which naloxone was given to patients taking opiates for pain, in which dose-related increases in laxative effects were observed (pages 245-249). However, there is no indication that prevention or elimination of constipation occurred.

3) The amount of direction or guidance presented and the presence or absence of working examples: The present specification does not outline examples showing that naloxone prevents or eliminates oxycodone-induced constipation. It is known in the art, as evidenced by the MiNicols et al. review, that opioid antagonists such as naloxone are effective treatments for constipation, but there is no indication that naloxone prevents constipation from ever occurring.

4) The quantity of experimentation necessary: In order to determine if naloxone prevents oxycodone induced constipation from ever occurring, one would have to administer naloxone and observe that constipation never happens. As

discussed by McNicols et al., naloxone dose-dependently treats constipation in most patients, but does not completely abolish constipation in all patients.

Claim Rejections – 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-6, 16-17 and 21 rejected under 35 U.S.C. 103(a) as being unpatentable over Oshlack et al. (US Patent 7,144,587).

Oshlack et al. teach solid dosage forms of compositions comprised of an opiate, an opiate antagonist and a hydrocolloid containing excipient (meeting the limitation of claim 1; Col. 6, lines 16-20). More specifically the opiates are chosen from agents such as morphine, codeine and oxycodone (meeting the limitation of claims 2-3; see Col. 12, lines 34-56 for a more complete list). Antagonists that are useful in the invention include naltrexone and naloxone (meeting the limitation of claims 4-5; lines 14-15). Dosage forms are taught that include coated beads including the opiate antagonist (meeting the limitation of claim 6; Col. 17, lines 23-61). In regards to the limitation that the amount of the enteric coated opiate antagonist pellets is effective to prevent opiate induced constipation, it would be obvious that because Oshlack et al. teach coated beads, it would necessarily prevent opiate induced constipation. It is taught that gelling

agents or other excipients are included in the dosage forms, which include starch and starch derivatives, lactose, xanthan gum, locust bean gum, microcrystalline cellulose, alginates, dicalcium phosphate (dibasic calcium phosphate) and magnesium stearate (Col. 7, lines 20-47; Col. 16, lines 48-55 and Example 6). It is noted that the teaching of dicalcium phosphate renders the monocalcium phosphate obvious because the compounds are similar and have similar properties of being excipients. Selection of a known material based on its suitability for its intended use is obvious absent a clear showing of unexpected results attributable to the Applicant's specific selection. See e.g., *In re Leshin*, 227 F.2d 197, 125 USPQ 416 (CCPA 1960). The gelling agents impart a gel-like quality to the dosage form if it is tampered with and prevent abuse of the dosage form by minimizing absorption (Col. 7, lines 48-55). It is further taught that when the dosage form is tampered with and exposed to a small amount of a liquid such as water, the dosage form will be unsuitable for injection (meeting the limitation of claim 18; Col. 3, lines 12-16). Table 1 exemplifies a composition comprised of oxycodone with naloxone. Further, Oshlack et al. teaches that the opiate/opioid antagonist formulation together with a hydrocolloid can be formulated in immediate release formulations or controlled release in any suitable tablet (Col. 17, lines 12-15), and teaches coated beads that can contain the opiate, the opiate antagonist and hydrocolloid. Therefore, it would be obvious that one tablet could contain beads that are controlled and immediate release (meeting the limitation of claim 16-17). Further, because Oshlack et al. teach compositions comprised of the same components, it

would be obvious that the composition would be released in the same areas, such as the colon (further addressing claim 16).

Oshlack et al. does not specifically teach a compound comprised of all the ingredients listed in claim 1.

However, it would be obvious to a person having ordinary skill in the art at the time of the invention to formulate a composition comprised of an opiate, an opiate antagonist, hydrocolloids and other excipients as exemplified in claim 1 because Oshlack et al. teach the suitability of all of the hydrocolloids and excipients in a composition of coated beads with an opiate and an opiate antagonist. One would be motivated to include the hydrocolloids and excipients in the composition in an effort to form a composition that when tampered with will impart a gel-like quality to avoid abuse of the opiate composition (as taught by Oshlack et al., Col. 7, lines 48-55).

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Renee Claytor whose telephone number is (571)272-8394. The examiner can normally be reached on M-F 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Renee Claytor

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